Amendments to the Specification

Please replace the paragraph at page 21, lines 15 through 31 with the following amended paragraph:

As described in Example 3, the inventors have also discovered a mutation in the EPM2B gene in dogs with Lafora's disease. In particular, all affected dogs studied had a bi-allelic expansion of a dodecamer repeat, termed D, and having the sequence GCCGCCCCCCGC (SEQ ID NO: 5) that starts at nucleotide number 1001 of canine EPM2B sequence shown in SEQ ID NO : 3. The inventors have shown that this 12 nucleotide repeat is specific to the canid superfamily, which includes dogs, wolves, foxes, coyotes, and jackals, and have shown that this repeat predisposes dogs to a massive sequence expansion, which is destructive to the EPM2B gene and causes Lafora disease. The inventors have thus discovered that canids, including dogs, are predisposed to Lafora Epilepsy. Accordingly, the invention further provides a method of detecting Lafora's disease in a canid comprising detecting a repeat of the sequence GCCGCCCCCCGC (SEQ ID NO : 5) which starts at nucleotide number 1001 in the canine sequence of EPM2B (SEQ ID NO : 3). In one embodiment, the method involves detecting at least 3 repeats, preferably at least 10 repeats, more preferably from about 14 to about 26 repeats in SEQ ID NO : 5.

Please replace the paragraph at page 46, lines 5 through 30 with the following amended paragraph:

Information and amplification conditions on the established (D6S274, D6S285, D6S966, D6S1567, D6S1678, D6S1688, D6S1959) and new (BV012563, BV012730, BV012565, BV012566, BV012568) are found in the UniSTS and Entrez Nucleotides database (http:/www.ncbi.nim.nih.gov/). DNA Sequence variations were detected by sequencing of PCR-products. To screen *EPM2B*, two sets of primer pairs that amplify overlapping fragments were used *EPM2B*-1F: (5'-ACTGTGACCGTG ACCGAGA-3')(SEQ ID NO: 53) and *EPM2B*-1R: (CACACCCCAAGGTAAGGAGA-3')(SEQ ID NO: 54); *EPM2B*-2F: (5'-GACTGCCATGTGGTTGTCAC-3')(SEQ ID NO: 55) and *EPM2B*-2R: (5'-AAACAATTCATTMTGGCAGCA-3') (SEQ ID NO: 56) (see FIG. 1). PCR was performed on 50 ng of DNA in buffer [75 mM Tris-HCl (pH 8.8), 20 mM (NH4)2SO4, 0.01% Tween 20, 1.5

mM MgCl2, 1M Betaine, 0.2 mM dNTP, 0.2 uM of each primer, 2.5 Units of Taq Polymerase (MBI Fermentas)]. Cycling conditions were: initial denaturation at 94°C. for 3 min followed by 35 cycles of denaturation at 94°C. for 30 sec, annealing at 60°C. for 30 sec and extension at 72°C. for 30 sec, with a 10 min final extension at 72°C. PCR products were purified using mircroCLEAN (Microzone Ltd). 3 µl (100 ng/µl) of purified PCR product was used as sequencing template. For all reactions, 1µl (5 pmol) of primer, 1.5µl 5X sequencing buffer (Applied Biosystems), 1µl BigDye Terminator v3.1, and 7.5µl H2O in a 14µl reaction volume were used. Thermocycling (MJ Research, Inc.) conditions were denaturing at 96°C. for 30s; annealing at 50° for 20s; and extension at 60°C. for 4 min; 35 cycles. All reactions were subsequently purified using multiscreen-HV filter plates (Millipore) and analyzed using an ABI-3700. All sequence variants detected in LD patients were examined in a collection of 50 (100 chromosomes) randomly selected DNA samples.

Please replace the paragraph at page 47, lines 1 through 21 with the following amended paragraph:

Gene annotation data and EST sequences were mainly obtained from the University of California Santa Cruz (UCSC) genome browser (http://genome.ucsc.edu/) and Celera Genomics (http://www.celera.com/). Additional putative genes were annotated using the Genescript algorithm (http://tcag.bioinfo.sickkids.on.ca/genescript/) and multi-species VISTA (http://www-gsd.lbl.gov/vista/) alignments between human and mouse sequence. The RING finger domain was predicted by Pfam, Prosite, InterProScan, SMART and MotifScan. NHL domains were identified using Pfam and InterProScan. EPM2B orthologues were identified using BLASTN and BLASTP analyses against the GenBank non-redundant database. Prediction of the sub-cellular localization of malin by sequence analysis was performed using PSORT II. No significant signal peptide sequence (for recognition of ER, Golgi complex, lysosome and integral plasma membrane proteins), mitbchondriail targeting sequence, nuclear localization signal and peroxisomal targeting signal was identified. The human multiple-tissue blot I and human brain blot II (Clontech) were probed with a [^{32}P]dCTP-labeled probe that was generated using the primers 5'-GTCACCATCACCMCGACTG-3' (SEQ ID NO: 57) and 5'-TGCGAAAGACCATGAGTGAC-3' (SEQ ID NO: 58), which amplified a 557 bp fragment

within the coding region of EPM2B. Hybridization and washing conditions were performed according to the manufacturer's instructions.

Please replace the paragraph at page 47, lines 23 through page 48, line 17 with the following amended paragraph:

The myc-tagged *EPM2A* transcript A expression construct (pcDNA3myc*EPM2A*), which encodes the cytoplasmic isoform of laforin has been described (24). A myc-tagged *EPM2B* construct was generated (pcDNA3mycEPM2B) using the same general protocols. Full-length *EPM2B* was amplified by PCR from genomic DNA using the (forward) primer (5'-gqatccATGgcggccgaagc-3') (SEQ ID NO: 59) containing a *BamHl* restriction site (underlined) and the start codon (uppercase) and a (reverse) primer (5'-gcgqccqcacaattcaftaatggcagac-3') (SEQ ID NO: 60)(SEQ ID NO: 60) containing a Notl site (underlined). This product was cloned into the corresponding sites of the mammalian expression vector pcDNA3 (Invitrogen). Myc was then introduced, in frame, after amplifying from a previous myc-containing vector with 5' *Kpnl*-tagged and 3' *BamHl*-tagged primers. pcDNA3myc*EPM2A* and pcDNA3myc*EPM2B* (2 mg) were transfected into Cos-7 cells using Lipofectamine-Plus (Invitrogen) and exposed to lipid-DNA complex in DMEM (Sigma-Aldrich) for 5 hours. Forty-eight hours post-transfection, cultures were rinsed twice in PBS and fixed for 15 min at -20.degree. C. in an acetone:methanol (1:1) mix. They were then stained with antibodies against myc-laforin and ER marker GRP94. Cultures were blocked for 1 hour (10% BSA/PBS) and incubated with anti-Myc and anti-ER for 45 min at room temperature. Slides were washed with PBS and incubated with secondary antibody (FITC-labeled goat anti-mouse, 1:400, detectable through the green filter; Texas red-labeled donkey anti-goat, 1:400, detectable through the red filter; Jackson ImmunoResearch Laboratories) in blocking solution. Following mounting (Dako Anti-Fade), they were analyzed by immunofluorescence light microscopy. For electron microscopic examination biopsy material was obtained from the LD patient and placed into chilled Universal fixative. Using standard protocols it was then analyzed at the ultra-structural level.